THE RELATION BETWEEN THE PHYSICAL STATE OF BRAIN CELLS AND BRAIN FUNCTIONS,—EXPERIMENTAL AND CLINICAL.

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The brain in all animals (including man) is but the clearing-house for reactions to environment,—for animals are essentially motor or neuro-motor mechanisms, composed of many parts, it is true, but integrated by the nervous system. Throughout the phylogenetic history of the race the stimuli of environment have driven this mechanism, whose seat of power—the battery—is the brain.

Since all normal life depends upon the response of the brain to the daily stimuli, we should expect in health as well as in disease to find modifications of the functions and the physical state of the component parts of this central battery—the brain cells. Although we must believe, then, that every reaction to stimuli, however slight, produces a corresponding change in the brain cells, yet there are certain normal, that is, non-diseased conditions which produce especially striking changes. The cell changes due to the emotions, for example, are so similar, and in extreme conditions approach so closely to the changes produced by disease, that it is impossible to say where the normal ceases and the abnormal begins.

In view of the similarity of brain cell changes, it is not strange that in the clinic as well as in daily life, we are confronted constantly by outward manifestations so nearly identical that the true underlying cause of the condition is too often overlooked or misunderstood. In our laboratory experiments and our clinical observations we have found that exhaustion from intense emotion, from prolonged physical exertion, from insomnia, from intense fear, certain toxemias, hemorrhage, and the conditions commonly denominated sur-

FIG. 1. Area from cerebellum, rabbit, normal.

gical shock, produce similar outward manifestations and identical brain cell changes.

It is, therefore, the purpose of this paper to present the definite results of certain laboratory researches which show certain relations between the alteration in brain functions and alterations in the brain cells.

Fear.—Our experiments showed that the brain cell changes due to fear may be divided into two stages: First, that of hyperchromatism—stimulation; second, that of hypochromatism—exhaustion. Hyperchromatism was shown only in the presence of the activating stimuli or within a very short time after they had been received. This state gradually changed until the period of maximum exhaustion was reached, about six hours later. Then a process of reconstruction began and continued until the normal state was again reached.

Fatigue.—Fatigue from overexertion produced in the brain cells like changes to those produced by fear, these changes being proportional to the amount of exertion. In the extreme stage of exhaustion from this cause we found that the total quantity of Nissl substance was enormously reduced. If the exertion is too greatly prolonged, it may take weeks or months for the cells to be restored to their normal condition. In fact, in exhaustion from the emotions or from physical work a certain number of brain cells are permanently lost. This probably explains the fact that an athlete or a race horse trained to the point of highest efficiency can but once in his life reach his maximum record. Under certain conditions, however, it may be possible that though some chromatin is forever lost, the remainder may be so remarkably developed that for a time at least it will compensate for that which is gone.

Hemorrhage.—The loss of blood from any cause, if sufficient to reduce the blood pressure, will occasion a change in the brain cells, provided the period of hypotension lasts more than five minutes. This time limit is a safeguard against permanent injury from the temporary hypotension which causes one to faint. If the hemorrhage is long continued and the blood pressure is low, there will be a permanent loss of some of the brain cells. This is why an indi-

vidual will never again be restored to his original powers after suffering from a prolonged hemorrhage.

Drugs.—According to their effect upon the brain cells, drugs may be divided into three classes: First, those that stimulate brain cells to increased activity,—as strychnine; second, those that chemically

Fig. 2. Area from cerebellum, rabbit, during fright.

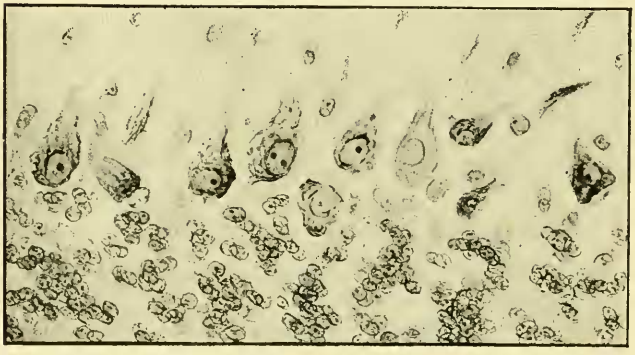

Fig. 3. Area from cerebellum, rabbit, 6 hours after fright.

destroy the brain cells,—as alcohol and iodoform; third, those that suspend the functions of the cells without damaging them,—as nitrous oxide, ether, morphia. Our experiments showed that brain cell changes induced by drugs of the first class are precisely the same as the cycle of changes produced by the emotions and physical

FIG. 4. Area from cerebellum, delirium tremens.

activity. We found that strychnia, according to the dosage, caused convulsions ending in exhaustion and death; excitation followed by lassitude; stimulation without notable after results; or increased mental *tone*. The brain cells accurately displayed these physiologic alterations in proportional hyperchromatism in the active stages, and proportional chromatolysis in the stages of reaction. The biologic and therapeutic application of this proof is as obvious as it is important.

Alcohol in large and repeated dosage caused marked morphologic changes in the brain cells which went as far even as destruction of the cells. Ether, on the other hand, even after five hours of administration, produced no observable destructive changes in the cells.

The effect of iodoform was peculiarly interesting, as it was the only drug that produced fever. Its observed effect upon the brain cells was that of widespread destruction.

Infections.—In every observation on dogs and on man pyogenic infections caused definite and demonstrable lesions in certain cells of the nervous system, the changes in the cortex and the cerebellum being most marked. For example, in infections the result of bowel obstruction, in peritonitis, and in osteomyelitis causing death, the real lesion is in the brain cells. The lassitude, diminished mental power, excitability, irritability, restlessness, delirium and unconsciousness that may be associated with acute infections, we may reasonably conclude are due to physical changes in the brain cells.

Graves' Disease.—In Graves' disease the brain cells showed marked changes which were apparently the same as those produced by overwork, by the emotions, and by strychnine. In one advanced case it was found that the brain had lost permanently a large number of cells. This is the reason undoubtedly why a severe case of exophthalmic goitre sustains such a permanent loss of brain power.

Insomnia.—The brains of rabbits which had been kept awake for 100 hours showed precisely the same changes as those shown in physical fatigue, strychnine poisoning and exhaustion from emotional stimulation. Eight hours of continuous sleep restored all the cells except those that had been completely exhausted. This will explain the permanent effect of long-continued insomnia;—that is,

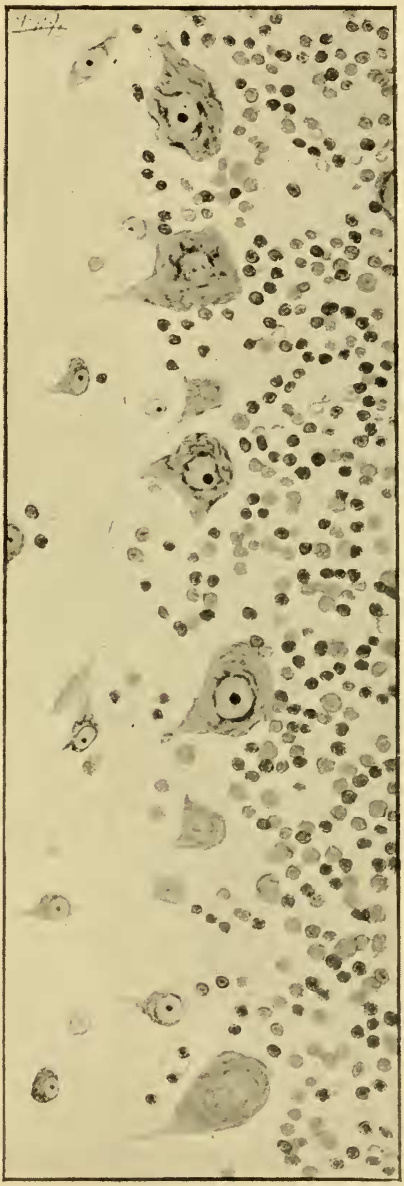

FIG. 5. Area from cerebellum, iodoform poisoning.

long-continued insomnia permanently destroys a part of the brain cells just as do too great physical exertion, certain drugs, emotional strain, exophthalmic goitre or hemorrhage. We found, however, that if instead of natural sleep the rabbits were placed for the same number of hours under nitrous oxide anesthesia, not only were the brain cells prevented from physical deterioration, but that 90 per cent. of them became hyperchromatic. This gives us a possible clue to the actual chemical effect of sleep. For since nitrous oxide owes its anesthetic effect to its influence upon oxidation, we may

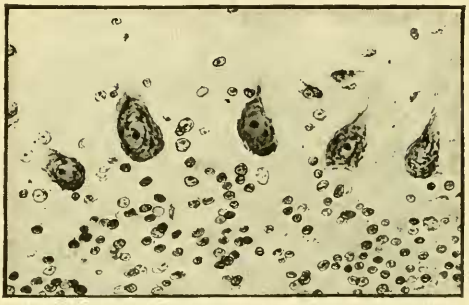

Fig. 6. Area from cerebellum, woodchuck, hibernating.

infer that sleep also is a question of oxidation of the cell content. If this is true, then it is probable that inhalation anesthetics exert their peculiar influence upon that portion of the brain through which sleep itself is produced. If nitrous oxide anesthesia and sleep are chemically identical, then we have a further clue to one of the primary mechanisms of life itself; and as a practical corollary one might be able to produce artificial sleep very closely resembling normal sleep, and with this advantage,—that by using an anesthetic interfering with oxidation the brain cells might be reconstructed after physical fatigue, after emotional strain, or after the depression of disease.

In the case of the rabbit in which nitrous oxide was substituted for sleep the appearance of the brain cells resembled those in but one other group experimentally examined,—the hibernating woodchucks.

Insanity.—Our researches have shown that in the course of a fatal disease and in fatal exhaustion, however produced, death does not ensue until there is marked disorganization of the brain tissue. In the progress of disease or exhaustion one may see in different patients every outward manifestation of mental deterioration —manifestations which, in a person who does not show any other sign of physical disease, mark him as insane. Take, for example, the progressive mental state of a brilliant scholar suffering from typhoid fever. On the first day of the gradual onset of the disease he would notice that his mental power was below its maxi-

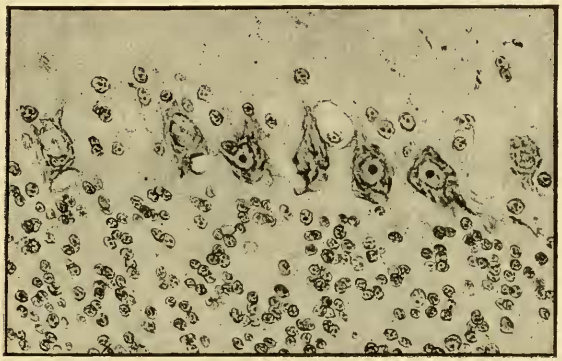

Fig. 7. Area from cerebellum, woodchuck, after fright.

mum efficiency; on the second he would notice a further deterioration, and so the mental effect of his disease would progress until he would find it impossible to express a thought or to make a deduction. No one can be philanthropic with jaundice; no one suffering from Graves' disease can be generous; no mental process is possible in the course of the acute infectious diseases. Just prior to death from any cause everyone is in a mental state which if it could be continued would cause that individual to be judged insane. If the delirium that occurs in the course of certain diseases could be continued the patient would be judged insane. In severe cases of Graves' disease the patient is insane. Individuals may be temporarily insane under overwhelming emotion. Every clinician has seen great numbers of

cases of insanity as phases of a disease, of an injury, or of an emotion. The stage of excitation in anesthesia is insanity. The only difference between what is conventionally called insanity and the fleeting insanity of the sick and the injured is that of time. We may conclude, therefore, what must be the brain picture of the person who is permanently insane. This *a priori* reasoning is all that is possible, since the study of the brain in the insane has thus far been wholly on the brains of those who have died of some disease. And it is impossible to say which changes have been produced by the fatal disease, and which by the condition producing insanity. The only logical way of investigating the physical basis of insanity would be to make use of the very rare opportunity of studying accidental death in the insane.

Our experiments have proved conclusively that whether we call a person fatigued or diseased, the brain cells undergo physical deterioration, accompanied by loss of mental power. Even to the minutest detail we can show a direct relationship between the physical state of the brain cells and the mental power of the individual,—that is, the physical power of a person goes *pari passu* with his mental power. Indeed, it is impossible to conceive how any mental action, however subtle, can occur without a corresponding change in the nerve cells. It is possible now to measure only the evidences of gross and violent mental activity on the brain cells. At some future time it will doubtless be possible to so refine the technique that more subtle changes may similarly be measured. Nevertheless, with the means at our disposal we have shown already that in all these conditions the cells of the cortex showed the greatest changes; and that loss of the higher mental functions accompanied the cell deterioration.

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